

REMARKS/ARGUMENTS

Claims 1-18 are pending in the instant application. Claims 1-18 stand rejected. Claims 8 and 11 are objected to because of informalities. Claims 1-18 stand rejected under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter related to which radicals can be used. Claims 13-18 stand rejected under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter related to which samples to use. Claims 7 and 14 are rejected because of insufficient antecedent basis. Claims 1-17 stand rejected under 35 USC 102(b) as being anticipated by Jørgensen et al. US 5,599,522. Claims 1-18 stand rejected under 35 USC 102(b) as being anticipated by Bednarek et al. Claims 1-18 stand rejected under 35 USC 102(b) as being anticipated by Hall et al.

Amendments:

Claims 1-12 directed to a radical for use in a DNP process have been cancelled.

Claims 13-18 have been amended to a Process of DNP. Basis for this is found on page 6 of the specification (of WO2004/092759 hereinafter).

Claim 13 has been further amended to more particularly point out and distinctly claim the subject matter which the applicant regards as the invention, by combining it with the subject matter of former claim 4, and by specifying that the sample comprises NMR active nuclei.

Basis for this last amendment is found on page 1, second paragraph of the specification.

Claims 19-25 have been added, directed to a process of DNP. The subject matter of former claims 4-12 have been included in these claims so the basis is found therein as well as on pages 2 and 3 of the specification.

Claim objections:

Former claims 8 and 12 were objected to because of informalities. These claims have been cancelled. New claim 21, including subject matter of former claim 8, has been written such that there are no periods after “tert”. New claim 24, including subject matter of former claim 12, has been written to include a hyphen after 1,2.

Claim rejections – 35 USC 112:

Claims 1-18 stand rejected under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter related to which radicals can be used. Claims 1-12 have been cancelled. Claim 13 has been amended by specifying that the radical is generated from a radical precursor being a photolabile organic compound or an organic compound comprising a photolabile group, and that the radical is generated by photolysis. The claim also states that the radical decomposes from about 5 K to about 273 K. Hence, applicant believes both physical and chemical features of the radical have been provided. The applicant has also amended the claim to more clearly show that a process is claimed, and request that the claims 13-25 are examined as process claims.

Claims 13-18 stand rejected under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter related to which samples to use. The rejected claims have been amended to point out that the sample comprises NMR active nuclei. As it should be clear that the claims are directed to a process, and both the radical and the sample are further defined, the applicant request that the claims are examined as process claims and that the rejection is withdrawn.

Claims 7 and 14 are rejected because of insufficient antecedent basis. Claim 7 has been cancelled. The subject matter of former claim 7 has been included in claim 20 and antecedent basis has been corrected such that the claim refers to claim 19. Claim 14 has been amended specifying that the generation of the radical is carried out outside a DNP magnet. Reconsideration is respectfully requested.

Claim Rejections – 35 USC § 102

The inventors of the instant application have identified that there is a need for paramagnetic compounds for use in a DNP process which effect high polarisation of the sample. It has been found that the use of radicals, which are generated in situ from a radical precursor and decompose to non-radical species at temperatures from about 5 K to about 273 K is especially useful for the dynamic nuclear polarisation of a sample and the subsequent NMR analysis of said sample. The present invention hence provides a process for dynamic nuclear polarisation of a sample wherein radicals are generated in situ from radical precursors and decompose to non-radical species at temperatures from about 5 K to about 273 K. The

radicals according to the invention are stable during the DNP process as the DNP temperature is generally very low, preferably about the temperature of liquid helium (4.2 K) or less, more preferably 1.5 K or less, especially preferably 1 K or less. As the NMR analysis of the sample is generally carried out at temperatures above the DNP temperature, preferably above 273 K, particularly preferably at room temperature, there are no radicals present in the sample during the NMR analysis. Hence, problems due to the presence of radicals like broadening of the NMR signals, loss of sensitivity, low resolution of the spectrum and rapid loss of polarisation can be avoided.

Claims 1-17 stand rejected under 35 USC 102(b) as being anticipated by Jørgensen et al. US 5,599,522. The patent discloses stable free radicals (col. 1 line 5) having a long half life, e.g. being a stable radical for at least one minute at ambient temperature (col. 2, line 53-58). The term “ambient temperature” denotes temperatures in the room temperature range, i.e. temperatures from about 18 to 24 °C (291 to 297 K). The stable free radicals of Jørgensen are intended to be used as imaging agents/contrast media in MR imaging (col. 1, lines 2-3), hence they must be stable at temperatures where MR imaging is carried out on a human patient. This temperature range is clearly well above the temperature range of 5 to 273 K (-268 to 0 °C) used in the claimed process of the present application. The radicals used in the claimed process are not stable above 273 K (0 °C), they decompose to non-radical species and are hence not suitable for the purpose described by Jørgensen.

Hence claim 13 is novel over Jørgensen and so are the dependent claims as all are containing the feature that the radicals used decompose to non-radical species at temperatures from 5 to 273 K and thus are novel over Jørgensen.

Claims 1-18 stand rejected under 35 USC 102(b) as being anticipated by Bednarek et al. Bednarek is directed to generation of hydroperoxyl radicals by γ -irradiation of glassy water. There is no teaching of a process for DNP of a mixture comprising a sample and a radical, wherein the sample comprises an NMR active nuclei, and wherein the radical is generated *in situ*, as now claimed. Hence, claims 13-25 as claimed are novel over Bednarek.

Claims 1-18 stand rejected under 35 USC 102(b) as being anticipated by Hall et al., (Science 276 (1997), 930-932). Hall discloses the use of the nitroxide radical 4-amino-TEMPO in a DNP process. TEMPO is a stable free radical which is commercially available in its free radical form. Nothing by Hall indicates that TEMPO is generated *in situ*. Further, 4-amino-TEMPO does not decompose in the temperature range of 5 to 273 K, but is stable as a free radical. For shipping and storage, it is recommended to keep the compound refrigerated, i.e. at temperatures around 4 °C. This means that 4-amino-TEMPO is stable at a temperature of 4 °C whereas the radicals used in the claimed process of the present invention are decomposed to a non-radical species at a temperature of 0 °C.

Hence, as the DNP process described in claim 13 and the dependent claims contain the features that the radicals used are generated *in situ* and decompose to non-radical species at temperatures from 5 to 273 K these are novel over Hall.

Favorable reconsideration of claims 13-25 is respectfully requested.

CONCLUSION

In view of the amendments and remarks herein, Applicants believe that each ground for rejection made in the present application has been successfully overcome, and that all the pending claims, 13-25, are in condition for allowance.

The Examiner is invited to telephone the undersigned in order to resolve any issues that might arise and to promote the efficient examination of the current application.

Respectfully submitted,

/Craig Bohlken/

Craig Bohlken
Reg. No. 52,628

GE Healthcare, Inc.
101 Carnegie Center
Princeton, NJ 08540
Phone (609) 514-6530